suspension or solution. This suspension or solution can then be sprayed onto the surface of the API particles to form a coating of film by evaporation of the solvent or water. Examples of technologies for wet particle coating include microencapsulation, fluid bed coating, spray drying, pan coating etc. In dry particle coating (also referred to as solventless coating), API particles are physically coated with fine particles of inactive ingredients (polymer and additives) to form particle composites. Examples of dry particle coating include hot melt coating, supercritical coating, impaction coating, electrostatic coating. API particles coated with a taste-masking inactive ingredient may provide a more pleasant experience for a patient having difficulties swallowing or having a sensitivity to taste that would otherwise lead to a negative patient experience and poor compliance.

[0006] For example, a dry, solventless mixing method may use high energy vibrations or acoustic resonance to mix the API with the inactive ingredient(s). Further, coating an API particle with a functional coating may temporarily delay the release of the API in a patient's mouth during dispersion of the pharmaceutical composition, yet still allow at least 90% of the API that would be released without the coating to be released from the functionally-coated API within a suitable amount of time for absorption. Coating the API in a taste-masking inactive ingredient allows the dissolution rate of the coated API particle to be controlled such that a majority of the API is not released until after the coated API particle has passed to a patient's stomach.

SUMMARY

[0006a] In an aspect of the present disclosure, there is provided a pharmaceutical composition comprising:

65-85 % w/w API particles;

15-30 % w/w coating material encapsulating the API particles; and

3-15 % w/w matrix surrounding the coated API particles, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 25°C and at least 60 % relative humidity.

[0006b] In another aspect of the present disclosure, there is provided a pharmaceutical composition prepared by a process comprising the steps of:

coating API particles with a coating material to form coated API particles, wherein the coating material comprises one or more deformable components;

applying mechanical stress to the coated API particles to deform the one or more deformable components;

coating the coated API particles with silica;

applying mechanical stress to at least one of adhere, partially embed, or embed the silica on the coated API particles;

sieving the coated API particles to remove excess coating material, wherein the excess coating material comprises coating material not bound to a coated API particle;

mixing the coated API particles into a matrix solution/suspension to form a pharmaceutical suspension; and

dosing the pharmaceutical suspension into a mold, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 25°C and at least 60 % relative humidity.

[0006c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition disclosed herein, for use in administering to a patient.

[0006d] In another aspect of the present disclosure, there is provided a method of preparing a pharmaceutical composition comprising:

coating API particles with a coating material to form coated API particles, wherein the coating material comprises one or more deformable components;

applying mechanical stress to the coated API particles to deform the one or more deformable components;

coating the coated API particles with silica;

applying mechanical stress to at least one of adhere, partially embed, or embed the silica on the coated API particles;

sieving the coated API particles to remove excess coating material, wherein the excess coating material comprises coating material not bound to a coated API particle;

mixing the coated API particles into a matrix solution/suspension to form a pharmaceutical suspension; and

dosing the pharmaceutical suspension into a mold.

[0007] Provided are methods for minimizing agglomeration of coating material for coated API particles produced using various mixing processes. API particles that are coated using conventional mixing processes often experience agglomeration of excess coating material, particularly upon storage. Agglomeration of coating material can decrease the stability of the pharmaceutical product over time. For example, a pharmaceutical product's disintegration

time may increase over time if it comprises agglomerated coating material. An increased disintegration times and/or a decreased dissolution rate implies an unstable pharmaceutical product. An unstable pharmaceutical product can lead to a shorter shelf life than desired. Accordingly, examples provided may help minimize agglomeration of coating material for coated API particles to improve the stability of the pharmaceutical product during storage and to increase its shelf life.

[0008] For example, methods described include removing excess coating material from the coated API particles to minimize the possibility of agglomeration of the coating material particles. Particularly, methods provided include sieving the coated API particles such that the final pharmaceutical product is adequately surrounded by dry matrix, minimizing any agglomeration of coating material particles upon storage. Pharmaceutical compositions described provide for a disintegration time and a dissolution rate that remain relatively stable over time.

[0009] In some examples, a pharmaceutical composition is provided, the pharmaceutical composition comprising: 65-85 % w/w API particles; 15-30 % w/w coating material coating the API particles; and 3-15 % w/w matrix surrounding the coated API particles, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 25°C and at least 60 % relative humidity. In some examples, the coating material comprises a first coating material and a second coating material and the pharmaceutical composition comprises 10-30 % w/w the first coating material and 0.5-10 % w/w the second coating material. In some examples, the first coating material comprises wax. In some examples, the second coating material comprises silica. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 30°C and at least 65 % relative humidity. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 40°C and at least 75 % relative humidity. In some examples of the pharmaceutical composition, the API particles comprise one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants. In some examples of the pharmaceutical composition, the coating material comprises silica as one or more of a protectant or a flow aid. In some examples of the pharmaceutical composition, wherein the coating material comprises a wax. In some examples of the pharmaceutical composition, the coating material comprises one or more of carnauba wax, candelilla wax, or synthetic wax. In some examples of the pharmaceutical composition, a coating ratio used to combine the API particles with the coating material comprises 5-85% w/w coating material and 15-95% w/w uncoated API particles. In some examples of the pharmaceutical composition, the matrix comprises a matrix former and a structure former. In some examples of the pharmaceutical

composition, the matrix former comprises one or more of a water soluble material, a water dispersible material, a polypeptide, a polysaccharide, polyvinyl alcohol, polyvinylpyrrolidone, and acacia. In some examples of the pharmaceutical composition, the matrix former comprises a polypeptide. In some examples of the pharmaceutical composition, the polypeptide comprises gelatin.In some examples of the pharmaceutical composition, the structure former comprises one or more of mannitol, dextrose, lactose, galactose, and cyclodextrin. In some examples of the pharmaceutical composition, the structure former comprises mannitol.

[0010] In some examples, a pharmaceutical composition is provided, the pharmaceutical composition prepared by a process comprising the steps of: coating API particles with a first coating material to form coated API particles, wherein the coating material comprises one or more deformable components; applying mechanical stress to the coated API particles to deform the one or more deformable components; coating the coated API particles with silica; applying mechanical stress to embed the silica into the coated API particles; sieving the coated API particles to remove excess coating materials, wherein the excess coating materials comprise coating materials not bound to a coated API particle; mixing the coated API particles into a matrix solution/suspension to form a pharmaceutical suspension; and dosing the pharmaceutical suspension into a mold, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 25°C and at least 60 % relative humidity. In some examples of the pharmaceutical composition, a dosing ratio used to combine the coated API particles with the matrix solution/suspension comprises 5-60 % w/w coated API particles to 40-95 % w/w matrix solution/suspension. In some examples of the pharmaceutical composition, a coating ratio used to combine the API particles with the coating material comprises 5-85 % w/w coating material and 15-95 % w/w uncoated API particles. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises freezing the dosed suspension under sub-zero conditions and freeze-drying to form a lyophilized pharmaceutical composition. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 30°C and at least 65 % relative humidity. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 40°C and at least 75 % relative humidity. In some examples of the

pharmaceutical composition, the pharmaceutical composition comprises 65-85 % w/w API particles. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises 15-30 % w/w coating material. In some examples of the pharmaceutical composition, the pharmaceutical composition comprises 3-15 % w/w matrix. In some examples of the pharmaceutical composition, the method used to prepare the pharmaceutical composition comprises sieving uncoated API particles. In some examples of the pharmaceutical composition, sieving the coated API particles comprises passing the coated API particles through a device comprising two or more sieves. In some examples of the pharmaceutical composition, sieving the coated API particles comprises sieving the coated API particles to an average particle size of 75 μm or greater. In some examples of the pharmaceutical composition, sieving the coated API particles comprises sieving the coated API particles to an average particle size of 200 μm or less. In some examples of the pharmaceutical composition, the API particles comprise one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants. In some examples of the pharmaceutical composition, the coating material comprises silica as one or more of a protective coat or a flow aid. In some examples of the pharmaceutical composition, the one or more deformable components of the coating material comprises a wax. In some examples of the pharmaceutical composition, the wax comprises one or more of carnauba wax, candelilla wax, or synthetic wax. In some examples of the pharmaceutical composition, the matrix comprises a matrix former and a structure former. In some examples of the pharmaceutical composition, the matrix former comprises one or more of a water soluble material, a water dispersible material, a polypeptide, a polysaccharide, polyvinyl alcohol, polyvinylpyrrolidone, and acacia. In some examples of the pharmaceutical composition, the matrix former comprises a polypeptide. In some examples of the pharmaceutical composition, the polypeptide comprises gelatin. In some examples of the pharmaceutical composition, the structure former comprises one or more of mannitol, dextrose, lactose, galactose, and cyclodextrin. In some examples of the pharmaceutical composition, the structure former comprises mannitol.

[0011] In some examples, a method of treating a patient is provided, the method comprising administering to a patient a therapeutic amount of the pharmaceutical composition. In some examples of the method, the patient is a human.

[0012] In some examples, a method of preparing a pharmaceutical composition is provided, the method comprising: coating API particles with a first coating material to form coated API particles, wherein the coating material comprises one or more deformable components; applying mechanical stress to the coated API particles to deform the one or more deformable components of the coating material to form a continuous film layer over the surface of the API particles; coating the coated API particles with silica to form a second coat by applying mechanical stress to partially embed or embed the silica into the deformable coat; sieving the coated API particles to remove excess coating materials; mixing the coated API particles into a matrix solution/suspension to form a pharmaceutical suspension; and dosing the pharmaceutical suspension into a mold. In some examples of the method, a dosing ratio used to combine the coated API particles with the matrix solution/suspension comprises 5-60 % w/w coated API particles to 40-95 % w/w matrix solution/suspension. In some examples of the method, a coating ratio used to combine the API particles with the coating material comprises 5-85 % w/w coating material and 15-95 % w/w uncoated API particles. In some examples of the method, the method comprises freezing the dosed suspension under sub-zero temperatures and freeze-drying to form a lyophilized pharmaceutical composition. In some examples of the method, the method comprises sieving uncoated API particles. In some examples of the method, sieving the coated API particles comprises passing the coated API particles through a device comprising two or more sieves. In some examples of the method, sieving the coated API particles comprises sieving the coated API particles to an average particle size of 75 μm or greater. In some examples of the method, sieving the coated API particles comprises sieving the coated API particles to an average particle size of 200 μm or less. In some examples of the method, the API particles comprise one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants. In some examples of the method, the coating material comprises silica as one or more of a protective coating or a flow aid. In some examples of the method, the one or more deformable components of the coating material comprises a wax.

[0013] In some examples of the method, the wax comprises one or more of carnauba, candelilla wax, or synethetic wax. In some examples of the method, the matrix comprises a matrix former and a structure former. In some examples of the method, the matrix former comprises one or more of a water soluble material, a water dispersible material, a polypeptide, a polysaccharide, polyvinyl alcohol, polyvinylpyrrolidone, and

acacia. In some examples of the method, the matrix former comprises a polypeptide. In some examples of the method, the polypeptide comprises gelatin. In some examples of the method, the structure former comprises one or more of mannitol, dextrose, lactose, galactose, and cyclodextrin. In some examples of the method, the structure former comprises mannitol.

BRIEF DESCRIPTION OF THE DRAWINGS

[0014] The invention will now be described, by way of example only, with reference to the accompanying drawings, in which:

[0015] Fig. 1A shows an API particle coated with particles of a deformable coating material (i.e., a first coating layer) according to some embodiments;

[0016] Fig. 1B shows an API particle coated with a continuous film layer of deformable coating material (i.e., a first coating layer) according to some embodiments;

[0017] Fig. 1C shows an API particle coated with a continuous film layer of deformable coating material (i.e., a first coating layer) with particles of silica (i.e., a second coating layer) partially embedded and/or embedded on the surface of the first coating layer according to some embodiments;

[0018] Fig. 2 shows a scanning electron microscope (SEM) image of an un-coated API particle according to some embodiments;

[0019] Fig. 3 shows an SEM image of a coated API particle according to some embodiments;

[0020] Fig. 4 is a flow chart of a mixing process for preparing coated API particles, according to some embodiments; and

[0021] Figs. 5A-5P are a series of photomicrographs taken of sieved coated API for Examples 1-8.

DETAILED DESCRIPTION OF THE INVENTION

[0022] Described herein are exemplary embodiments of methods for minimizing and/or preventing the agglomeration of the coating material of coated API particles. Particularly, methods according to some embodiments include removing excess coating material particles to minimize and/or to prevent agglomeration of coating material in a pharmaceutical product. In some embodiments, methods may include sieving the raw API particles and/or the coated

CLAIMS

1. A pharmaceutical composition comprising:

65-85 % w/w API particles;

15-30 % w/w coating material encapsulating the API particles; and

3-15 % w/w matrix surrounding the coated API particles, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 25°C and at least 60 % relative humidity.

2. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 30°C and at least 65 % relative humidity.

3. The pharmaceutical composition of claim 1 or 2, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 40°C and at least 75 % relative humidity.

4. The pharmaceutical composition of any of claims 1-3, wherein the API particles comprise one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants.

5. The pharmaceutical composition of any of claims 1-4, wherein the coating material comprises silica as one or more of a protective coating or a flow aid.

.6. The pharmaceutical composition of any of claims 1-5, wherein the coating material comprises a wax.

7. The pharmaceutical composition of any of claims 1-6, wherein the coating material comprises one or more of carnauba wax, candelilla wax, or synthetic wax.

8. The pharmaceutical composition of any of claims 1-7, wherein a coating ratio used to combine the API particles with the coating material comprises 5-85% w/w coating material and 15-95% w/w uncoated API particles.

9. The pharmaceutical composition of any of claims 1-8, wherein the matrix comprises a matrix former and a structure former.

10. The pharmaceutical composition of claim 9, wherein the matrix former comprises one or more of a water soluble material, a water dispersible material, a polypeptide, a polysaccharide, polyvinyl alcohol, polyvinylpyrrolidone, and acacia.

11. The pharmaceutical composition of claim 9 or 10, wherein the matrix former comprises a polypeptide.

12. The pharmaceutical composition of claim 10 or 11, wherein the polypeptide comprises gelatin.

13. The pharmaceutical composition of any of claims 8-12, wherein the structure former comprises one or more of mannitol, dextrose, lactose, galactose, and cyclodextrin.

14. The pharmaceutical composition of claim any of claims 8-13, wherein the structure former comprises mannitol.

15. A pharmaceutical composition prepared by a process comprising the steps of:

coating API particles with a coating material to form coated API particles, wherein the coating material comprises one or more deformable components;

applying mechanical stress to the coated API particles to deform the one or more deformable components;

coating the coated API particles with silica;

applying mechanical stress to at least one of adhere, partially embed, or embed the silica on the coated API particles;

sieving the coated API particles to remove excess coating material, wherein the excess coating material comprises coating material not bound to a coated API particle;

mixing the coated API particles into a matrix solution/suspension to form a pharmaceutical suspension; and

dosing the pharmaceutical suspension into a mold, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 25°C and at least 60 % relative humidity.

16. The pharmaceutical composition of claim 15, wherein a dosing ratio used to combine the coated API particles with the matrix solution/suspension comprises 5-60% w/w coated API particles and 40-95% w/w matrix solution/suspension.

17. The pharmaceutical composition of claim 15 or 16, wherein a coating ratio used to combine the API particles with the coating material comprises 5-85% w/w coating material and 15-95% w/w uncoated API particles.

18. The pharmaceutical composition of any of claims 15-17, comprising freezing the dosed suspension under sub-zero conditions and freeze-drying to form a lyophilized pharmaceutical composition.

19. The pharmaceutical composition of any of claims 15-18, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 30°C and at least 65 % relative humidity.

20. The pharmaceutical composition of any of claims 15-19, wherein the pharmaceutical composition comprises a disintegration time of less than 10 seconds for at least six months under storage conditions of at least 40°C and at least 75 % relative humidity.

21. The pharmaceutical composition of any of claims 15-20, comprising 65-85 % w/w API particles.

22. The pharmaceutical composition of any of claims 15-21, comprising 15-30 % w/w coating material.

23. The pharmaceutical composition of any of claims 15-22, comprising 3-15 % w/w matrix.

24. The pharmaceutical composition of any of claims 15-23, comprising sieving uncoated API particles.

25. The pharmaceutical composition of any of claims 15-18, wherein sieving the coated API particles comprises passing the coated API particles through a device comprising two or more sieves.

26. The pharmaceutical composition of any of claims 15-25, wherein sieving the coated API particles comprises sieving the coated API particles to an average particle size of 75 μm or greater.

27. The pharmaceutical composition of any of claims 15-26, wherein sieving the coated API particles comprises sieving the coated API particles to an average particle size of 200 μm or less.

28. The pharmaceutical composition of any of claims 15-27, wherein the API particles comprise one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants.

29. The pharmaceutical composition of any of claims 15-28, wherein the coating material comprises silica as one or more of a protective coating or a flow aid.

30. The pharmaceutical composition of any of claims 15-29, wherein the one or more deformable components of the coating material comprises a wax.

31. The pharmaceutical composition of any of claims 15-30, wherein the wax comprises one or more of carnauba wax, candelilla wax, or synthetic wax.

32. The pharmaceutical composition of any of claims 15-31, wherein the matrix solution/suspension comprises a matrix former and a structure former.

33. The pharmaceutical composition of claim 32, wherein the matrix former comprises one or more of a water soluble material, a water dispersible material, a polypeptide, a polysaccharide, polyvinyl alcohol, polyvinylpyrrolidone, and acacia.

34. The pharmaceutical composition of claim 32 or 33, wherein the matrix former comprises a polypeptide.

35. The pharmaceutical composition of any of claims 32-34, wherein the polypeptide comprises gelatin.

36. The pharmaceutical composition of any of claims 32-35, wherein the structure former comprises one or more of mannitol, dextrose, lactose, galactose, and cyclodextrin.

37. The pharmaceutical composition of claim any of claims 32-36, wherein the structure former comprises mannitol.

38. A pharmaceutical composition of any one of claims 15-37, for use in administering to a patient.

39. The pharmaceutical composition for use of claim 38, wherein the patient is a human.

40. A method of preparing a pharmaceutical composition comprising:

coating API particles with a coating material to form coated API particles, wherein the coating material comprises one or more deformable components;

applying mechanical stress to the coated API particles to deform the one or more deformable components;

coating the coated API particles with silica;

applying mechanical stress to at least one of adhere, partially embed, or embed the silica on the coated API particles;

sieving the coated API particles to remove excess coating material, wherein the excess coating material comprises coating material not bound to a coated API particle;

mixing the coated API particles into a matrix solution/suspension to form a pharmaceutical suspension; and

dosing the pharmaceutical suspension into a mold.

41. The method of claim 40, wherein a dosing ratio used to combine the coated API particles with the matrix solution/suspension comprises 5-60% w/w coated API particles and 40-96% w/w matrix solution/suspension.

42. The method of claim 41 or 42, wherein a coating ratio used to combine the API particles with the coating material comprises 5-85% w/w coating material and 15-95% w/w uncoated API particles.

43. The method of any of claims 40-42, comprising freezing the dosed suspension under sub-zero conditions and freeze-drying to form a lyophilized pharmaceutical composition.

44. The method of any of claims 40-43, further comprising sieving uncoated API particles.

45. The method f any of claims 40-44, wherein sieving the coated API particles comprises passing the coated API particles through a device comprising two or more sieves.

46. The method f any of claims 40-45, wherein sieving the coated API particles comprises sieving the coated API particles to an average particle size of 75 μm or greater.

47. The method of any of claims 40-46, wherein sieving the coated API particles comprises sieving the coated API particles to an average particle size of 200 μm or less.

48. The method of any of claims 40-47, wherein the API particles comprise one or more of anti-inflammatories, analgesics, anti-psychotics, anti-emetics, laxatives, anti-diarrheals, anti-histamines, or anti-depressants.

49. The method of any of claims 40-48, wherein the coating material comprises silica as one or more of a protective coating or a flow aid.

50. The method of any of claims 40-49, wherein the one or more deformable components of the coating material comprises a wax.

51. The method of any of claims 40-50, wherein the wax comprises one or more of carnauba wax, candelilla wax, or synthetic wax.

52. The method of any of claims 40-51, wherein the matrix solution/suspension comprises a matrix former and a structure former.

53. The method of claim 52, wherein the matrix former comprises one or more of a water soluble material, a water dispersible material, a polypeptide, a polysaccharide, polyvinyl alcohol, polyvinylpyrrolidone, and acacia.

54. The method of claim 52 or 53 wherein the matrix former comprises a polypeptide.

55. The method of claim 53 or 54, wherein the polypeptide comprises gelatin.

56. The method of any of claims 52-55, wherein the structure former comprises one or more of mannitol, dextrose, lactose, galactose, and cyclodextrin.

57. The method of any of claims 52-56, wherein the structure former comprises mannitol.